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| 10/550,267 | 02/13/2006 | Michael Soeberdt | 041165-9093-00 | 1396 |

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| EXAMINER | |
|---|---|
| LEESER, ERICH A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1624 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/550,267 | SOEBERDT ET AL. | |
| | Examiner | Art Unit | |
| | Erich A. Leeser | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-14 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *September 20, 2005 and April 24, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-14 are currently pending in this application and under examination.

### *Priority*

Acknowledgement is made that this application is a 371 of PCT/EP04/02907, filed March 19, 2004, which claims benefit of EPO 03006254.1, filed on March 20, 2003.

### *Information Disclosure Statement*

The references cited in the IDS, dated September 20, 2005 and April 24, 2006, are made of record.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for preventing disorders, diseases or conditions responsive to the modulation of the melanocortin-4 receptor, cancer cachexia, muscle wasting, anorexia, anxiety and/or depression, obesity, diabetes, male or female sexual dysfunction or erectile dysfunction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope

with these claims. Applicants' claims are not enabled for preventing any of the possible diseases or conditions which could possibly be modulated by the melanocortin-4 receptor. The only established prophylactics are vaccines not the substituted piperidine and piperazine derivative compounds such as are present here. In addition, it is presumed that prevention of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before infection occurs. This would require extensive and potentially open-ended clinical research on healthy subjects. 2) Applicants intend to prevent diseases or conditions modulated by the melanocortin-4 receptor. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to clinical pharmaceutical medicine and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become infected before the fact. 6) The artisan using Applicants' invention would be a Board Certified physician in CNS, oncological, orthopaedic, urogical or gynecological diseases or conditions with an MD degree and several years of experience. Despite intensive efforts,

pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent a disease or condition generally. That is, the skill is so low that no compound effective generally against diseases or conditions modulated by melanocortin-4 receptor has ever been found let alone one that can prevent such conditions. 7) It is well-established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by formula (I).

The Examiner suggests deletion of the word "prevention" to obviate this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The following apply.

Claims 5-14 are rejected because this claim is of **indeterminate scope** as no particular disease or condition is ever recited. Such claim language reciting a particular mode of action(s)

may read on diseases that are affected by melanocortin-4 receptor activity in ways not yet understood. What interaction qualifies as "responsive" and how does one determine a host in need of such treatment/prevention? What distinguishes a mammal, the apparent host, in need of such response versus one who is not in need? Additionally, determining whether a given disease responds or not to such modulation would involve much experimentation since a negative response from one patient does not mean the drug is not useful as no drug has 100% effectiveness. Thus what success rate determines if a particular method is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 U.S.C. § 112, second paragraph is whether Applicant has clearly defined the invention (in light of the specification), *not* what may be discovered by future research as this type of claim language clearly requires.

### *Claim Rejections 35 U.S.C. § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 10-11 and 14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fotsch, et al., WO 03/009847.

Fotsch, et al., teaches substituted piperidine compounds for the purpose of modulating the melanocortin receptor. Generically, claim 1 of the reference covers the scope of instant claim 1 when the reference's R is alkyl, q is 1; $R^{1a}$ to $R^{1f}$ and $R^a$ are all hydrogen; k is 1; $R^6$ is aryl or heteroaryl; Y is –NH-; and $R^2$ is f), and $R^8$ is a) heterocyclyl substituted with oxo, and instant A is piperidine; X is alkyl; Y is hydrogen; m is 0 or 1; Ar is aryl or heteroaryl; n is 0. The first paragraph of p. 53 in specification states: "Preferred heterocyclic radicals include five to ten membered fused or unfused radicals." As such, "heterocyclyl" encompasses the benzopyran of instant $R_1$. In addition, $-N(R^9)_2$ of the reference can be hydrogen which encompasses instant $R_4$ and $R_5$. Note compound 263 found on page 172 of the reference. This compound is the closest exemplified compound of the reference. It differs from the compounds of the reference by having quinoline where the compounds of the reference teach benzopyran, nitrogen versus oxygen.

The instant claimed compounds would have been obvious, because one skilled in the art would have been motivated to prepare compounds similar to those taught in the reference with the expectation of obtaining compounds which could be used to treat obesity and diabetes mellitus. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Erich A. Leeser/

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